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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/774,076	02/06/2004	Nicholas F. Landolfi	05882.0064.NPUS01	7347

27194 7590 03/11/2005

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EXAMINER	
KIM, YUNSOO	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 03/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/774,076	LANDOLFI ET AL.	
	Examiner	Art Unit	
	Yunsoo Kim	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-45* is/are pending in the application.

4a) Of the above claim(s) *11,12,17,27,29-31 and 33-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,13,14,16,18-26,28 and 32* is/are rejected.

7)☒ Claim(s) *15* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/24/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

1. The Examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Yunsoo Kim, Art Unit 1644, Technology 1600.

2. Applicant's amendment, filed 12/9/04 is acknowledged.

Claims 1-4, 10,18-26 and 28 have been amended.

Claims 11, 12 and 17 have been cancelled.

Claims 1-10, 13-16, 18-45 are pending.

3. Applicant's election without traverse of Group I (claims 1-10, 13-16, 18-26, 28 and 32) with a species election of anti-AR antibody HuPAR34 in the reply filed on 12/9/04 is acknowledged. However, the species is free of the art. The prior art search was extended to the next species.

Claims 11, 12, 17, 27, 29-31 and 33-45 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

Claims 1-10, 13-16; 18-26, 28 and 32 are under consideration in the instant application.

4. Sequence compliance: The instant application appears to be in sequence compliance for patent applications containing nucleotide sequence and/or amino acid sequence disclosures.

5. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged.

6. Applicant's IDS, filed 11/24/04 is acknowledged. However, the references 7-25 and 30 have not been considered. Applicant fails to provide the foreign documents and the non-patent literature.

7. The use of the trademarks "Lipofectamine 2000" on p.37, line 1, "EpiLife", "CellTiter-Glo" on p.42, lines 5, 8, "pCR4Blunt-TOPO" on p.42, line 26, and "sepharose" on p.45, line 31 have been noted in the specification of the instant application. It should be accompanied by the ® symbol wherever it appears and be accompanied by the generic terminology.

8. Claim 1 is objected to because of the following informalities: In the second line, AR should be spelled out and contains "th", a typographic error. Appropriate correction is required.

9. Claim 15 is objected by being depended upon rejected claim.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 3, 16 and 26 are indefinite in the recitation of PAR34, PAR80, and HuPAR34 because the characteristics are not known. The use of PAR34, PAR80 or HuPAR34 anti-AR antibody as the sole means of identifying the claimed antibody renders the claims indefinite because PAR34, PAR80, and HuPAR34 are merely laboratory designations which do not clearly define the claimed product, since different laboratories my use the same laboratory designations to define completely distinct antibodies.

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 1-10, 13-14, 16, 18-26, 28 and 32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a chimeric or human antibody that competitively inhibits binding of an amphiregulin (AR) peptide to anti-AR antibody that consists of SEQ ID NOs: 2, 3, 4, 5, 12 or 14 to treat psoriasis, does not reasonably provide enablement for antibody fragments that competitively inhibit binding of an AR, at least 80% identical or at least 98% identical or polymeric, allelic variants, mutant, interspecies homolog or conservatively modified variant sequence to SEQ ID NO:1 to anti-AR antibody or any antibody fragments, or any chimeric or human antibody consisting of at least 60% identical to the SEQ ID NO: 2, 3, 4; 5, 12, or 14 to treat cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification does not provide a sufficiently enabling description of the claimed invention.

There is insufficient guidance in the specification as filed as to how the skilled artisan would make and use the fragments and percent identical to sequences in the instant claims. A person of skill in the art would not know which fragments are essential, which fragments are non-essential, and what particular lengths identify essential fragments. There is insufficient guidance to direct a person of skill in the art to select particular fragment is essential for antigen binding. Without detailed direction as to which fragment is essential to antigen binding, a person of skill in the art would not be able to determine which fragments are antigen binding without undue experimentation.

It is well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity which is characteristic of the parent immunoglobulin. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites. Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al (Proc Natl Acad Sci USA 1982 Vol 79 page 1979). Rudikoff et al. teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function. It is unlikely that fusion proteins as defined by the claims which may contain less than the full complement of CDRs from the heavy and light chain variable regions of an IFN-a antibody in unspecified order and fused to any human or nonhuman framework sequence, have the required binding function.

Furthermore, Applicant has no working examples demonstrating an antibody fragment or at least 60% identical to SEQ ID NOs:2, 3, 4, 5, 12, or 14 or any antibody or antibody fragments to variant, mutants to at least 80% identical to SEQ ID NO:1 would inhibit binding of AR polypeptide and anti-AR antibody and to treat cancer.

To summarize, reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view of the quantity of experimentation necessary, the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breath of the claims, it would take undue trials and errors to practice the claimed invention.

14. Claims 1-10, 13-14, 16, 18-26, 28 and 32 are rejected under 35.U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of an antibody to a polypeptide consisting of SEQ ID NO:1; and a chimeric antibody that competitively inhibits binding of an AR peptide to anti-AR antibody that consists of SEQ ID NOs: 2, 3, 4, 5, 12 or 14; however, applicant is not in possession of any antibody fragments that competitively inhibit binding of an AR, at least 80% identical or at least 98% identical or polymeric, allelic variants, mutant, interspecies homolog or conservatively modified variant sequence to SEQ ID NO:1 to anti-AR antibody or any antibody fragments, or any chimeric or human antibody consisting of at least 60% identical to the SEQ ID NO: 2, 3, 4, 5, 12, or 14. There are $1.1x\ 10^{34}$ possible combinations of amino acid sequences for at least 80% identical to SEQ ID NO:1 alone without possible combinations of antibody fragments into consideration.

There is insufficient written description encompassing "mutant", "polymorphic variant", "allelic variant" or "conservatively modified variant sequence" because any amino acid sequence of different chemical or physical properties of amino acid is not set forth in the specification as filed, commensurate in scope with the claimed invention. Therefore, Applicant does not possess the scope of claimed invention. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of use.

Consequently, conception in either case cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See Fiers v. Revel, 25 USPQ2d 1601,1606 (CAFC 1993).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

16. Claim 10 is rejected under 35 U.S.C. 102(e) as being anticipated by Sato et al. (U.S.Pat. No, 6,677,436).

Sato et al. teach humanized antibodies having 80 % identical to a heavy chain variable region of SEQ ID NO:2 and 80% identical to a light chain variable region SEQ ID NO:14 (see sequence listings SEQ ID NOs: 93, 99, 107, 140, 143, 144, 153, 154, 157, 158, 180, and 182 for sequence homology, col. 6, lines 35-39, col. 8, lines 3-13, and col. 15, lines 8-18).

Thus, reference teachings anticipate the instant claimed invention.

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. Claims 18-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shoyab et al. (US Pat No. 5,830,995) in view of Kaplan et al. (U.S.Pat No. 4,668,629).

Shoyab et al. teach a monoclonal antibody to any epitope of AR polypeptide (see SEQ ID NO:7). Shoyab et al. further teach the antibody fragments, (col. 15, lines 43-51), increased AR expression in tumor cells (col. 13, lines 45-56), blocks cell growth (col. 14, lines 38-49), neutralizing activity (col. 13, lines 57-60), conjugation to effector moiety for labeling (col. 24, lines 40-65) and competition of ligand binding (col. 31, lines 49-67).

The claimed invention differs from the reference teachings only by the recitation of human antibody.

However, Kaplan et al. teach how to make human monoclonal antibodies and the advantages of using human monoclonal antibodies in therapy as human monoclonal antibodies are less immunogenic (col. 4, lines 51-64).

It would have been obvious to one of the ordinary skill in the art at the time the inventions was made to employ the human monoclonal antibodies taught by Kaplan et al. in the monoclonal antibody to treat psoriasis taught by Shoyab et al. to make the therapy more attainable and effective by having less immunogenic human monoclonal antibody.

One of the ordinary skill in the art at the time the invention was made would have been motivated to do so because the teachings of Kaplan et al. is an obvious way to improve the therapy more effective and less immunogenic as in the claimed invention. Thus, it is expected to combine teachings above to enhance the atherosclerosis therapy as in claimed invention.

From the combined teachings of references, one of ordinary skill in art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of the ordinary skill in the art at the time the invention was made, as evidenced by references, especially in the absence of evidence to the contrary.

19. No claim is allowed.

20. It is noted that claims drawn to the following antibodies would appear to be free of the art:

1) an antibody comprising the heavy chain variable region defined by SEQ ID NO:2 and the light chain variable region defined by SEQ ID NO:3;
2) an antibody comprising the heavy chain variable region defined by SEQ ID NO:4 and the light chain variable region defined by SEQ ID NO:5; and
3) an antibody comprising a heavy chain variable region defined by SEQ ID NO:12 and a light chain variable region defined by SEQ ID NO:14.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yunsoo Kim whose telephone number is 571-272-3176. The examiner can normally be reached on Monday thru Friday 8:30 - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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February 25, 2005

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